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PCT



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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification<sup>6</sup>: <b>C12N 15/31, 5/18, 1/21, C07K 14/315, C12Q 1/68, A61K 39/09, G01N 33/569, 33/68</b></p>	<p><b>A3</b></p>	<p>(11) International Publication Number: <b>WO 98/18930</b></p> <p>(43) International Publication Date: 7 May 1998 (07.05.98)</p>
<p>(21) International Application Number: <b>PCT/US97/19422</b></p> <p>(22) International Filing Date: 30 October 1997 (30.10.97)</p> <p>(30) Priority Data: 60/029,960 31 October 1996 (31.10.96) US</p> <p>(71) Applicant (for all designated States except US): <b>HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).</b></p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): <b>KUNSCH, Charles, A. [US/US]; 2398B Dunwoody Crossing, Atlanta, GA 30338 (US). CHOI, Gil, H. [KR/US]; 11429 Potomac Oaks Drive, Rockville, MD 20850 (US). JOHNSON, L., Sydnor [US/US]; 13545 Ambassador Drive, Germantown, MD 20874 (US). HROMOCKYJ, Alex [US/US]; 10003 Sidney Road, Silver Spring, MD 20901 (US).</b></p> <p>(74) Agents: <b>BROOKES, A., Anders et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).</b></p>		<p>(81) Designated States: <b>AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</b></p> <p><b>Published</b></p> <p><i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 8 October 1998 (08.10.98)</p> <p><i>LKH JL</i></p>
<p>(54) Title: <b>STREPTOCOCCUS PNEUMONIAE ANTIGENS AND VACCINES</b></p> <p>(57) Abstract</p> <p>The present invention relates to novel vaccines for the prevention or attenuation of infection by <i>Streptococcus pneumoniae</i>. The invention further relates to isolated nucleic acid molecules encoding antigenic polypeptides of <i>Streptococcus pneumoniae</i>. Antigenic polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention additionally relates to diagnostic methods for detecting <i>Streptococcus</i> nucleic acids, polypeptides and antibodies in a biological sample.</p>		

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# INTERNATIONAL SEARCH REPORT

Intern: al Application No  
PCT/US 97/19422

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/31 C12N5/18 C12N1/21 C07K14/315 C12Q1/68  
A61K39/09 G01N33/569 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 06732 A (UNIV ROCKEFELLER ;MASURE H ROBERT (US); PEARCE BARBARA J (US); TUO) 9 March 1995 SEQ ID nos. 3 and 4 see claims 1-52	1-21
X	--- C. MARTIN ET AL.: "Relateness of penicillin-binding protein 1a genes from different clones of penicillin-resistant Streptococcus pneumoniae isolated in South Africa and Spain" EMBO J., vol. 11, no. 11, November 1992, OXFORD UNIVERSITY PRESS,GB;, pages 3831-3836, XP002060148 see the whole document --- -/-	1-15

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

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Date of the actual completion of the international search

6 May 1998

Date of mailing of the international search report

18. 08. 1998

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

Intern:      al Application No  
PCT/US 97/19422

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 16082 A (ASTRA AB ;BALGANESH TANJORE SOUNDARARAJA (IN); TOWN CHRISTINE MARY) 30 May 1996 SEQ ID nos. 5 and 6 see claims 1-26 ---	1-15
A	WO 95 31548 A (UAB RESEARCH FOUNDATION ;YOTHER JANET (US); DILLARD JOSEPH P (US)) 23 November 1995 see the whole document ---	1-21
A	WO 95 14712 A (RES CORP TECHNOLOGIES INC) 1 June 1995 see the whole document ---	1-21
A	WO 96 05859 A (AMERICAN CYANAMID CO) 29 February 1996 see abstract ---	1-21
A	WO 93 10238 A (US HEALTH) 27 May 1993 see the whole document ---	1-21
A	EP 0 687 688 A (UNIV OVIEDO ;UNIV LEICESTER (GB)) 20 December 1995 see abstract ---	1-21
A	EP 0 622 081 A (UAB RESEARCH FOUNDATION) 2 November 1994 see the whole document ---	1-21
A	B.J. PEARCE ET AL.: "Genetic identification of exported proteins in Streptococcus pneumoniae" MOLECULAR MICROBIOL., vol. 9, no. 5, 1993, BLACKWELL, OXFORD, GB, pages 1037-1050, XP002060149 see the whole document -----	1-21

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/ 19422

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim 17 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see continuation-sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-21 partially (subject 1. on continuation-sheet)

### Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA 210

## 1. Claims: (1-21) partially

An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence from the group consisting of of: (a) a nucleotide sequence SEQ ID no.1 encoding the the amino acid sequence of the polypeptide SEQ ID no.2 shown in Table 1; or (b) a nucleotide sequence complementary to said nucleotide sequence in (a); an isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent conditions to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in (a) or (b), wherein said polynucleotide which hybridizes does not hybridize under stringent hybridization conditions to a polynucleotide having a nucleotide sequence consisting of only A or of only T residues; an isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence or an epitope-bearing portion of a polypeptide having an amino acid sequence of SEQ ID no.2 in (a); said epitope-bearing portion of a said polypeptide has an amino acid sequence listed in Table 2; a method of making a vector using said isolated nucleic acid molecule; said recombinant vector; a method of making a recombinant host cell using said vector; said recombinant host cell; a method of producing said polypeptide; said polypeptide; an isolated antibody that binds to said polypeptide; a hybridoma which produces said antibody; a vaccine comprising said polypeptide selected from SEQ ID no.2 in Table 1, or a fragment thereof; a method of preventing or attenuating an infection caused by a member of Streptococcus genus in animal using said polypeptide; a method for detecting Streptococcus nucleic acid sequences using the above-described nucleic acid probe; a kit for detecting Streptococcus antibodies in a biological sample using said polypeptide sequence;

## 2-113. Claims: (1-21) partially

-Idem as subject 1 but limited to the sequences having SEQ ID nos. 3 to 226. (Invention 2 is limited to SEQ ID nos. 3 and 4; Invention 3 is limited to SEQ ID nos. 5 and 6; ..... Invention 113 is limited to SEQ ID nos. 225 and 226).

For the sake of conciseness, the first group is explicitly defined, the other groups are defined by analogy hereto.



## INTERNATIONAL SEARCH REPORT

Information on patent family members

Patent Application No

PCT/US 97/19422

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9506732 A	09-03-95	AU 7680994 A	22-03-95
		CA 2170726 A	09-03-95
		EP 0721506 A	17-07-96
		FI 960977 A	30-04-96
		JP 9504686 T	13-05-97
		NO 960839 A	19-04-96
WO 9616082 A	30-05-96	AU 693537 B	02-07-98
		AU 2045895 A	18-01-96
		AU 3088795 A	17-06-96
		CA 2150532 A	02-01-96
		CN 1173182 A	11-02-98
		EP 0792284 A	03-09-97
		FI 972215 A	26-05-97
		GB 2290792 A	10-01-96
		HU 77487 A	28-05-98
		IE 950412 A	10-01-96
		NO 972353 A	01-07-97
		NZ 272242 A	26-03-96
WO 9531548 A	23-11-95	AU 2638595 A	05-12-95
		EP 0804582 A	05-11-97
WO 9514712 A	01-06-95	US 5474905 A	12-12-95
WO 9605859 A	29-02-96	US 5565204 A	15-10-96
		AU 3363695 A	14-03-96
		CA 2198251 A	29-02-96
		EP 0778781 A	18-06-97
		JP 10504717 T	12-05-98
WO 9310238 A	27-05-93	AU 3065892 A	15-06-93
EP 0687688 A	20-12-95	ES 2075803 A	01-10-95
		ES 2088820 A	16-09-96
		WO 9516711 A	22-06-95
EP 0622081 A	02-11-94	AU 682018 B	18-09-97
		AU 5769694 A	27-10-94
		CA 2116261 A	21-10-94

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 97/19422

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0622081 A		FI 941695 A	21-10-94
		JP 7126291 A	16-05-95
		NO 941420 A	21-10-94
		US 5679768 A	21-10-97
		ZA 9401584 A	12-10-94
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